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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/078,650	02/19/2002	Katsumi Fujimoto	14875-101001/C1-107PCT-US	7203

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EXAMINER	
MCKELVEY, TERRY ALAN	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 01/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/078,650	FUJIMOTO ET AL.	
	Examiner	Art Unit	
	Terry A. McKelvey	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *7,8 and 11-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,9,10 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/21/02; 5/9/03; 7/21/03.*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *sequence attachment*.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-6, 9-10, and 15, drawn to SEQ ID NO:1 and encoding SEQ ID NO:2 in the reply filed on 10/5/04 is acknowledged. The traversal is on the ground(s) that the three nucleotide and three amino acid sequences represent closely-related bHLH transcription factors and thus examination of all three nucleic acids can be made without serious burden. This argument is persuasive for SEQ ID NO:11 and encoding SEQ ID NO:12 because the sequences are so closely related that they can be searched together based upon the search of one nucleic acid. This is not found persuasive for SEQ ID NOS:13 and 14 because these sequences are not so closely related that a search for SEQ ID NO:1 would suffice for a complete search of SEQ ID NO: 13.

The applicant also argues that the search required for claim 1 parts (b), (c), and (e) of Group I is exactly the same as the search required for the proteins of Group II (claim 7) and thus examination of claim 7 with the Group I claims does not cause serious burden. This argument is not persuasive because the invention of Group II (claim 7) is classified in a separate class/subclass from the invention of Group I, which is prima

facie evidence of burden to search and examine together. The non-patent literature search is different too because a search for and identification of a protein in the prior art does not necessarily result in the identification of the nucleic acid encoding the protein because proteins are often isolated without the nucleic acid encoding the proteins, and nucleic acids encoding a protein are very often isolated without the isolation of the protein encoded by the nucleic acids. Thus, the identification of the protein or nucleic acid in the prior art would not complete the required search for the other until the other is also found in an additional search, or a continued search is determined to be exhaustive, finding that the other is not in the prior art. Additionally, should the protein be rejoined with the nucleic acids, then additional searching and examination drawn to methods of making and using the protein (drawn to 35 USC 112, first paragraph considerations) would be required as a part of rejoinder practice if the protein is allowable. This additional searching and examination resulting from rejoining the proteins to the elected claims would be burdensome.

The applicant argues that it is standard practice in the USPTO to include the method of producing a protein with the claims to the nucleic acid and thus it would not be a burden to

search and examine claim 8 with the elected claims. This argument is not persuasive because the principles of restriction are what is meant to be standard in the USPTO, not any particular groups of claim types being kept together because what one examiner would find to be burdensome to search and examine together in one case may not be burdensome in another set of claims in another case because the search and claims are different in every case and thus each case must stand and be examined on its own merits. No actual reason why there would be no burden in rejoining claim 8 is set forth. "Standard practice" in the USPTO allows restriction between products and methods of using products as set forth in the restriction requirement in the previous Office communication. It is acknowledged that standard rejoinder practice based upon allowable product claims will be followed.

The requirement is still deemed proper and is therefore made FINAL.

Claims 7-8 and 11-14 (and the parts of the elected claims drawn to SEQ ID NOS:13-14) are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/5/04.

Claim Rejections - 35 USC § 101 and 35 USC § 112, First Paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 9-10, and 15 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are directed to isolated nucleic acid selected from the group consisting of nucleic acids: comprising the coding region of a nucleotide sequence selected from SEQ ID NO:1 and 11 (elected), encoding a protein comprising SEQ ID NO:2 or 12 (elected), encoding a protein comprising a modified amino acid sequence which retains the biological activity of SEQ ID

NO:2 or 12, hybridizes under stringent conditions to a sequence selected from SEQ ID NO:1 and 11 and encoding a protein that retains the biological activity of SEQ ID NO:2 or 12, and encoding a partial peptide of a protein selected from SEQ ID NO:2 and 12. Vectors and transformants comprising the nucleic acids are also claimed, as are nucleic acids that comprise 15 or more nucleotides of SEQ ID NO:1 or 11.

There is no well established utility for the nucleic acids and encoded proteins because the nucleic acids and proteins are not completely described in the prior art and there is no specific function taught which is similar enough to a prior art nucleic acid or protein so as to support a well established utility.

The specification discloses that the protein encoded by the nucleic acids fits into a family of bHLH transcription factors each member of which are involved in different aspects of development and differentiation. This identification of the family is based upon only a limited degree of homology. However, the instant specification does not disclose any additional information regarding the protein such as what cell types express the protein or what the subcellular location is, timing of regulation of the protein during cellular differentiation, which hormones or transcription factors

regulate the protein, and what physiological or biochemical significance is possessed by the protein, such as what the target sites of the alleged transcription factor are. The specific biological activity of the protein and variants and fragments of the protein encoded by the nucleic acids as claimed are not taught.

The specification asserts the following utilities for the claimed nucleic acids, etc:

1. used as marker to determine developmental stages and cell differentiation.

2. used for diagnosis of diseases associated with the protein encoded by the nucleic acids.

3. used for prophylaxis and treatment of diseases associated with the protein encoded by the nucleic acids (i.e., gene therapy using the nucleic acids).

4. used in the development of pharmaceutical agents for various diseases associated with the protein.

5. used for in vivo or in vitro production of the protein, which protein can be used for purposes similar to those above, and for screening for a compound that binds to the protein which is a potential therapeutic for the diseases associated with the protein.

However, none of these asserted uses meet the three-pronged requirement of 35 USC 101 regarding utility, namely, that the asserted utility be credible, specific, and substantial. The asserted utilities will each be addressed in turn.

1. The specification does not teach what the specific developmental stages or cell differentiation is associated with the nucleic acid or protein and thus this asserted utility is not specific or substantial. Any protein or nucleic acid can potentially be a marker, but in the absence of the specific association of the nucleic acid or protein with a particular stage or differentiation state, there is no specificity and significant further experimentation is required to confirm the real world context of use of the nucleic acids as a marker for a stage or cell state.

2. and 3. The specification does not teach any specific disease that is specifically affected by the claimed nucleic acid or encoded protein. Although it is indicated that the protein may be associated with cartilages and arthritis, this is not a substantial utility because no specific nexus between this assertion and the claimed nucleic acids and encoded protein is taught. It would require significant further experimentation to confirm that the nucleic acid and protein is associated with what is alleged based upon no evidence showing the actual

association with the indicated diseases or tissues. Thus, use of the nucleic acids or encoded proteins for diagnosis or prophylaxis or treatment would require significant further experimentation to confirm the real world context of use for any of these uses.

4. Because the specification does not demonstrate that the nucleic acids and encoded proteins are specifically associated with any particular disease, there is no specific utility for developing pharmaceuticals based upon the nucleic acids or encoded proteins because any nucleic acids or proteins can be potentially used for development of pharmaceuticals, without specificity to a specific disease that is associated with the nucleic acids or encoded proteins. The utility is not substantial because significant further experimentation would be required to confirm the real world use of the nucleic acids or encoded proteins in making pharmaceutical agents.

5. The specification teaches that the nucleic acids can be used for the production of the encoded proteins. First, this is not true for all of the nucleic acids claimed. Second, this a specific, substantial, and credible utility only if the produced protein has a specific, substantial, and credible utility. Most of these asserted utilities are addressed above. The specification also asserts that the protein can be used for

screening for a compound that binds to the protein which is a potential therapeutic for the diseases associated with the protein. This is not a specific and substantial utility for essentially the same reasons set forth in item 4 above.

Claims 1-6, 9-10, and 15 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 1-6 and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to nucleic acids, etc as described in the rejection above. Thus, the claims are drawn to a genus of compounds that is defined in some of the instances partly by their function. These are the nucleic acids, etc that lack

written description: the ones that encode variants of SEQ ID NO:2 or 12 that retain the biological activity of the wild type sequences.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In the instant case, the only factor present in the claims is drawn to a partial structural limitation drawn to variants of the sequences that are set forth, but limited to those that have the biological function of the wild type SEQ ID NO:2 or 12. Because the specification fails to describe the specific biological function of the wild type proteins (which presumably are present in the proteins), the specification does not describe the structure of even one variant sequence which retains the biological activity. No assays are taught which would identify the encoded protein variants that retain the biological activity. There is no guidance as to the parts of the sequences that need to be unaffected in order to retain the biological activity of the

proteins. In the absence of this information, the structure of the proteins that have this unknown biological activity are equally unknown. Accordingly, in the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genus which encompasses variants of SEQ ID NO:2 or 12 which retains the biological activity of SEQ ID NO:2 or 12.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of nucleic acids or encoded proteins, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation or identification. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it.

The compound itself is required. See *Fiers v. Revel*, 25USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only nucleic acids that encode SEQ ID NO:2 or 12 or fragments thereof, but not the full breadth of the claims encompassing nucleic acids that encode variant proteins that retain the biological activity of SEQ ID NO:2 or 12 meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The use of "stringent conditions" renders the claims vague and indefinite because there is no clear art recognized definition of what constitutes "stringent" in this context, which varies between different references and different ones of those of skill in the art, resulting in the metes and bounds of the claimed nucleic acids being unclear. The specification fails to set forth a clear definition, instead setting forth one set of conditions as an example of conditions that are considered stringent, which clearly shows the intent to have the term encompass other conditions not set forth and thus the actual metes and bounds of the nucleic acids encompassed by the term are unclear.

Claim Rejections - 35 USC § 101

Claims 6 and 15 are rejected under 35 U.S.C. § 101 because the claimed invention is drawn to non-statutory subject matter. The preamble of the claims recites "A transformant carrying ...". Transformants read on both transformant cells and transformant organisms, including transformant human beings,

which are not statutory subject matter. Amending the claims to recite "A transformant cell ..." would be remedial. It should be noted that claims specifically drawn to transformant whole organisms that are not cells would be subject to restriction into a group separate from the elected group.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 9-10, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by NCI-CGAP (Accession AA996006/c).

NCI-CGAP teaches an isolated nucleic acid (a cDNA clone and corresponding mRNA) which comprises 100% sequence similarity to 322 contiguous nucleotides of SEQ ID NO:1 and SEQ ID NO:11. This reads on an isolated nucleic acid comprising at least 15 nucleotides, wherein the nucleic acid is completely complementary to a continuous region of at least 15 nucleotides in the sequence of SEQ ID NO:1 or 11. The isolated nucleic acid

taught by the reference encodes a partial peptide of a protein selected from SEQ ID NO:2 and 12, which corresponds to about amino acid 81 to about amino acid 188 of the two proteins. The nucleic acid also encodes a protein comprising an amino acid sequence of SEQ ID NO:2 or 12 because "an amino acid sequence" reads on less than the complete amino acid sequence of SEQ ID NO:2 or 12. The cDNA clone, insert length 496, is taught by the reference as being inserted into a vector which is transformed into the lab host DH10B, producing a transformant (which is actually what the library member taught by the reference comprises). See the features section of the reference.

Conclusion

No claims are allowed.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

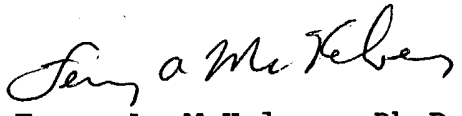
Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Terry A. McKelvey whose telephone number is (571) 272-0775. The examiner can normally be reached on Monday through Friday, except for Wednesdays, from about 7:30 AM to about 6:00 PM. A phone message left at this number will be

responded to as soon as possible (i.e., shortly after the examiner returns to his office).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached at (571) 272-0781.



Terry A. McKelvey, Ph.D.
Primary Examiner
Art Unit 1636

December 27, 2004